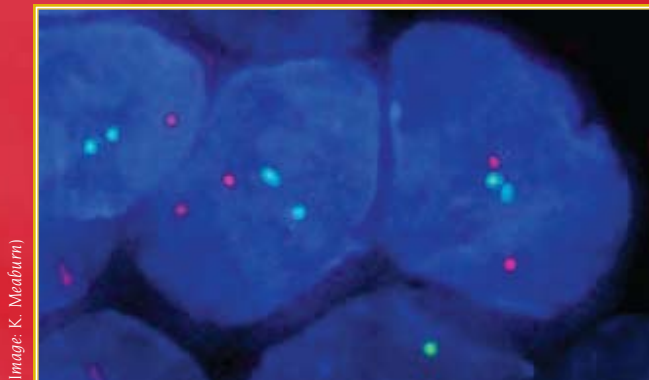
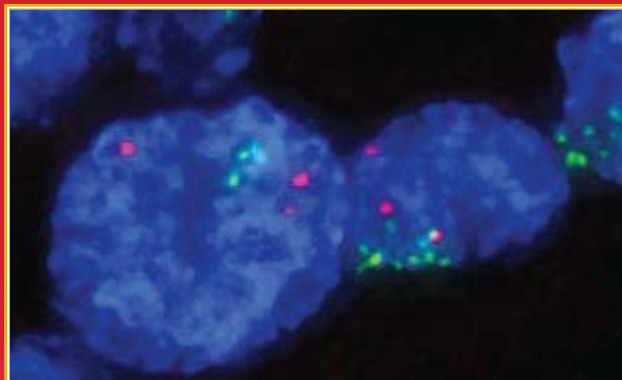


# Everything in Its Right Place

*Researchers identify genes that undergo spatial repositioning in breast cancer cells.*



(Image: K. Meaburn)



(Image: K. Meaburn)

Genes imaged using FISH in normal breast cells (*left*), and repositioned genes imaged in cancerous breast cells (*right*).

Understanding how gene abnormalities affect tumor formation and progression is important for tracing the mechanisms of disease and for developing diagnostic tools. Although a great deal of research has focused on the genetic mutations that drive cancer development, they are not the only signs of genetic havoc. A gene's spatial position may also be affected in certain cancers. Researchers have recently discovered that the spatial positioning patterns of genes within a cell nucleus may offer a new diagnostic strategy to distinguish cancerous from normal breast tissue.

"The reason why we started working on this is because we didn't know the mechanism for gene movement, which is a big question in the field," said Tom Misteli, Ph.D., Head of the Cell Biology of Genomes Group at CCR. "Everyone knows that certain genes change their position, but no one knows how. We still don't know why these things move, but they do. And that's all that matters for diagnostic purposes."

In a study published in the December 7, 2009 issue of the *Journal of Cell Biology*, Karen Meaburn, Ph.D., Dr. Misteli, and colleagues identified several genes

whose spatial position within the cell nucleus is altered in breast cancer when compared to normal tissue. The researchers used fluorescent *in situ* hybridization (FISH), a technique used to detect and localize specific DNA sequences, to visualize 20 genes in a set of 11 normal human breast tissue samples and 14 invasive cancer tissue samples, to determine if they occupy distinct intranuclear positions. They found eight genes that were frequently repositioned in cancer tissues and determined the repositioning events did not simply reflect genomic instability because repositioning did not correlate with changes in the number of gene copies in the cell.

The altered position of a single gene, *HES5*, which affects biological pathways that have been implicated in cancer, allowed identification of invasive breast cancer tissue with nearly 100 percent accuracy. Only a minority of tested genes underwent significant repositioning in a given cancer tissue, suggesting that repositioning is gene-specific and does not reflect a large-scale alteration in how the genome is organized within the nucleus. Furthermore, the scientists found

that several combinations of two or three genes allowed identification of cancerous tissues with low false-negative and false-positive rates.

This approach has advantages over current standard breast cancer diagnostic tests in that it gives a quantifiable readout and reduces human error. "This could be a useful first-line molecular test. Nowadays, breast cancers are diagnosed by pathologists, and this is very much based on their experience and on their background. In contrast, this would be a molecular test that you can actually quantitate very accurately."

The next step for Dr. Misteli and colleagues is to validate their approach on a larger number of samples and see how accurate this method could be for diagnostic purposes. If successful, this method of cancer diagnosis would not be limited to breast cancer, but could someday be applied to distinguish other types of tumors.

*To learn more about Dr. Misteli's research, please visit his CCR Web site at <http://ccr.cancer.gov/staff/staff.asp?Name=misteli>.*